DOCUMENT RESUME

ED 384 833 CG 026 285

| | |
|---|---|
| TITLE | Drugs and the Brain. |
| INSTITUTION | National Institutes of Health (DHHS), Bethesda, Md. |
| REPORT NO | NIH-Pub-91-3172 |
| PUB DATE | Jun 91 |
| NOTE | 28p.; Adapted from the "Medicine for the Public" series by the National Institutes of Health. Color illustrations may not copy well. |
| PUB TYPE | Reports - Descriptive (141) -- Guides - Non-Classroom Use (055) |
| EDRS PRICE | MF01/PC02 Plus Postage. |
| DESCRIPTORS | Behavior Patterns; *Brain Hemisphere Functions; Drug Abuse; *Drug Addiction; *Drug Education; Drug Rehabilitation; *Health Education; Illegal Drug Use; *Neurology; Physiology; *Substance Abuse |
| IDENTIFIERS | *Brain Functions |

ABSTRACT

This booklet explores various aspects of drug addiction, with a special focus on drugs' effects on the brain. A brief introduction presents information on the rampant use of drugs in society and elaborates the distinction between drug abuse and drug addiction. Next, a detailed analysis of the brain and its functions is given. Drugs target the more primitive portions of the brain, an action which allows them to override the cognitive processes of higher brain function. Explained is how pleasure acts as a powerful biological force to ensure survival, and how drugs act on the brain's pleasure cells. Drug addiction, it is argued, is a biologically based disease that actually alters the brain's pleasure networks. Discussed are how drugs interact with nerve cells in the brain and how drugs change the normal process of chemical neurotransmission. Finally, some of the special effects of different classes of drugs and the particular brain areas they target are examined. These include opiates, cocaine, marijuana, hallucinogens, PCP, depressants, and designer drugs. Other aspects of drug addiction are presented, such as the steps to addictions, the fetus and addiction, treatment, and genetics. (RJM)

**********
* Reproductions supplied by EDRS are the best that can be made *
* from the original document. *
**********

# Drugs and the Brain

ED 384 833

MEDICINE FOR THE PUBLIC

U.S. DEPARTMENT OF EDUCATION
Office of Educational Research and Improvement
EDUCATIONAL RESOURCES INFORMATION CENTER (ERIC)

- ☐ This document has been reproduced as received from the person or organization originating it.
- ☐ Minor changes have been made to improve reproduction quality.
- • Points of view or opinions stated in this document do not necessarily represent official OERI position or policy.

U.S. DEPARTMENT OF HEALTH
AND HUMAN SERVICES
Public Health Service
National Institutes of Health

CG026285

BEST COPY AVAILABLE

A list of Medicine for the Public booklets and videotapes is available by calling 301-496-2563 or by sending a postcard to:

Clinical Center Communications
National Institutes of Health
9000 Rockville Pike
Building 10, Room 1C255
Bethesda, Maryland 20892.

BEST COPY AVAILABLE

# Foreword

Americans continue to demand a greater role in deciding issues that affect their health. Increased health awareness and the convincing evidence linking lifestyle, risk factors, and specific diseases have accelerated our need to know.

The Clinical Center, recognizing the importance of providing information to facilitate intelligent decisions on health issues, created a unique lecture series featuring physician scientists working at the frontiers of biomedical research at the National Institutes of Health.

The Medicine for the Public series has provided an opportunity for millions of people to learn more about how their bodies work and what they can do to maintain or improve their health.

This publication is one of several adapted from the series. It is our sincere hope that you will find this material interesting and enlightening.

Saul Rosen, Ph.D., M.D.
Acting Director
Warren Grant Magnuson Clinical Center
National Institutes of Health

BEST COPY AVAILABLE

# Drugs and the Brain

## Introduction

We live in a world that sometimes seems saturated with drugs. If you have a headache, you take a pill. If you have a runny nose, you take another kind of pill. You cannot sleep very well? Well, there is a pill for that, too. Do you want to lose some weight or simply relax? You can take pills for all these things. Everywhere we turn, on the television and in the newspapers and magazines, we see advertisements that urge us to take some kind of drug for the myriad of problems, serious and superficial, which ail all of us.

So it should not be too surprising that, in addition to using legal drugs, people turn to illegal drugs or they abuse legal ones to try to solve their problems. People may be bored or anxious, or feel hopeless, and they turn to drugs to escape. Alcohol, tobacco, marijuana, cocaine, heroin, PCP, and a slew of other compounds do indeed change our moods and alter our perceptions. While some people are able to use some drugs in moderation, others cannot. They lose control of their drug-taking behavior and become addicted. Because drug abuse and addiction have become problems of significant consequence, it is important to understand why people abuse drugs and how drugs exert their addictive effects.

To begin with, we should bear in mind that drug abuse and drug addiction are entirely different phenomena. Drug abuse is a voluntary activity, but drug addiction is a compulsion. A drug abuser can choose whether or not to use a drug. People who are addicted, by contrast, have for all intents and purposes lost their free will to decide whether or not to use drugs. They feel they have no more choice about using drugs than they do about eating or breathing.

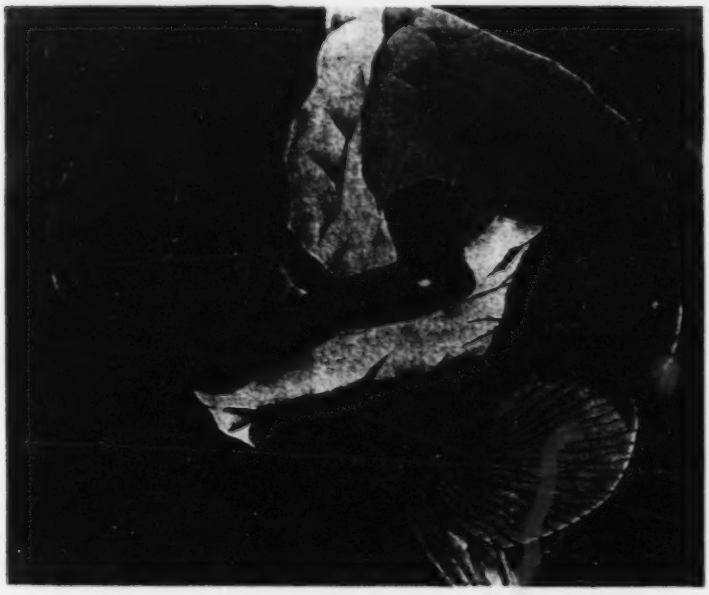
How can certain drugs produce such overpowering effects? The key lies in how these drugs affect the brain and some of its networks of nerve cells. To understand how drugs influence the brain, we need to examine some of the constituents of the brain and how they work.

## The Brain and Its Nerve Cells

The brain can be divided into several large regions, each responsible for some of the activities vital for living. The brain's lowest portion, called the brain stem, controls basic functions such as heart rate, breathing, eating, and sleeping. When one of these basic needs must be fulfilled, the brain stem structures can direct the rest of the brain and body to work toward that end. While these structures may be simple, they can exert powerful effects on our behavior.

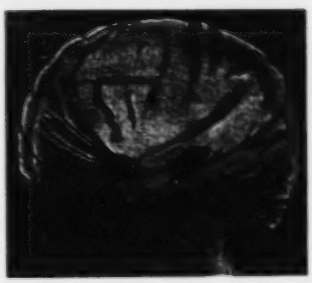
Above the brain stem and encompassing two-thirds of the human brain mass are the two hemispheres of the cerebral cortex. It is the cortex, the convoluted outer covering of nerve cells and fibers, that is the most recent part of the brain to evolve, developing completely only in mammals. Because they have a cortex, all mammals have more complex behavioral repertoires than creatures with simpler brains, like birds and reptiles. But, it is the large size and increased complexity of the human cerebral cortex that makes us different even from other mammals.

Though the cells throughout the entire extent of the cerebral cortex are remarkably similar, the cortex can be divided into dozens of specific areas, each with a highly specialized function. It is like a collection of small computers,



each working on a different aspect of a large problem. Much of the cerebral cortex is devoted to our senses—enabling us to see, hear, smell, taste, and touch. Other areas give us the ability to generate complex movements; still other regions allow us to speak and understand words, and different regions altogether allow us to think, plan, and imagine.

On top of the brain stem and buried under the cortex, there is another set of more primitive brain structures called the limbic system. These limbic system structures are crucial for connecting the cortex, which deals mainly with the outside world, with our emotions and motivations, which reflect our internal environment and survival needs. These connections allow us to experience a wide range of feelings and to influence these feelings with our perceptions and actions. They also enable us to use our impressive cognitive abilities to help us do the things we need to do to survive. Two large limbic structures, called the hippocampus and the amygdala, are also critical for memory. Sensory information flows from the cortex to these primitive brain regions, which take into account what is going on inside the brain and body and then instruct the cortex to store what is important.



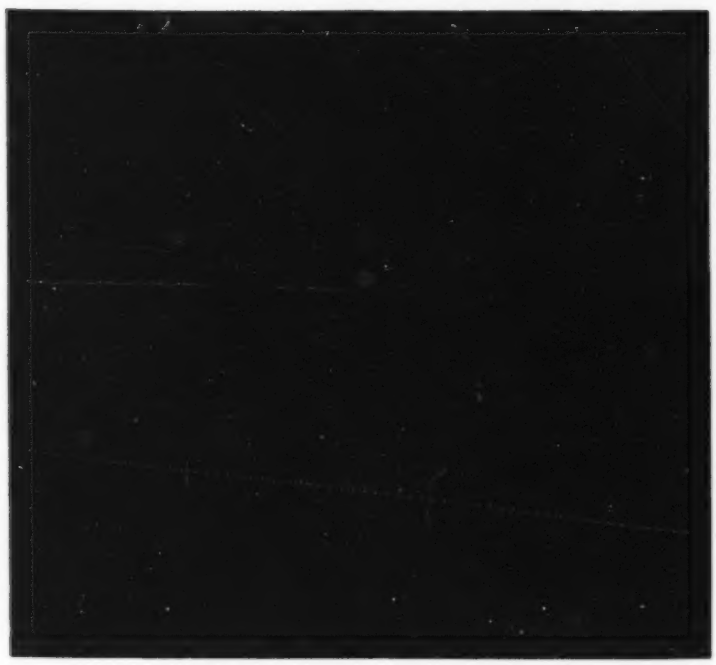
One of the reasons that drugs of abuse can exert such powerful control over our behavior is that they act directly on the more primitive brain stem and limbic structures, which can override the cortex in controlling our behavior. In effect, they eliminate the most human part of our brain from its role in controlling our behavior.

Surprisingly, the feeling of pleasure turns out to be one of the most important emotions for our survival. In fact, the feeling of pleasure is so important that there is a circuit of specialized nerve cells devoted to producing and regulating it. One important set of these nerve cells, which uses a special chemical messenger, a neurotransmitter called dopamine, sits at the very top of the brain stem. These dopamine-containing neurons relay messages about pleasure through their nerve fibers to nerve cells in a limbic structure called the nucleus accumbens. Still other fibers reach to a related part of the frontal region of the cerebral cortex. So, the pleasure circuit spans the survival-oriented brain stem, the emotional limbic system, and the complex information processor called the cerebral cortex.

The reason that pleasure, which scientists call reward, is a powerful biological force for our survival is that pleasure reinforces any behavior that elicits it. If you do something pleasurable, the brain is wired so that you tend to do that again. This is why a rat or a monkey so readily learns to press a lever for food. The animal does it because it is reinforcing—pressing the lever gets food and eating the food turns on the pleasure center, an action that helps ensure that the animal will do again what got him that food in the first place. And all of this happens unconsciously. We do not have to think about it or pay attention. It is an automatic brain function.

Thus, life's sustaining activities, such as eating a good meal or engaging in sex, activate this pleasure circuit. By doing so, they teach us to do these things again and again. But certain substances, including all the drugs that people abuse, also can potently activate the brain's pleasure circuit. Unfortunately, the more a person uses these drugs to get feelings of pleasure, the more the person learns to repeat the drug-taking behavior and the more the brain learns to depend on drugs to evoke pleasure.

So, that is the key reason why people repeatedly abuse drugs; drugs make them feel good by directly turning on



the pleasure circuit. It also is a reason why drug addiction is so difficult to treat; addicts find that only drugs can give them pleasure. Drug addiction is a biologically based disease that alters the way the pleasure center, as well as other parts of the brain, function. By directly turning on our pleasure circuits, many addictive drugs make our brains behave as if these compounds were as important for survival as food, sex, and all the other natural rewards that also turn on the pleasure circuits. Thus, drugs pervert to a destructive end a strong emotion that helps to activate one of the brain's most powerful learning mechanisms.

This is a general description of how drugs influence our behavior by working on one important brain center. To really understand how drugs produce their effects, however, we need to understand how nerve cells and the molecules that make up these cells interact with the molecules that make up drugs.

To do this, we need to examine the fine structure of nerve cells, the communications network of the brain. Each nerve cell, or neuron, contains three important parts. The central cell body directs all the activities of the neuron. Messages from other nerve cells are relayed directly to the cell body through a set of branches called dendrites. Having examined the information relayed to it by its dendrites, the cell body then can send messages out to its neighbors through a cablelike fiber called an axon. But the axon does not make direct contact with the dendrites of other neurons. A tiny gap separates the terminal of the axon, sending the message from the dendrites of the cell with which it seeks to communicate. This gap is called a synapse.

The message is sent across the synaptic gap between the two nerve cells by a chemical called a neurotransmitter. The little packets of the neurotransmitter are released at the end of the axon and diffuse across the gap to bind to special molecules, called receptors, that sit on the surface of the dendrites of the adjacent nerve cell.

When the neurotransmitter couples to a receptor, it is like a key fitting into a lock that starts the process information flow in that neuron. First, this coupling allows the receptor molecules to link with other molecules that extend through the cell membrane to the inside of the cell.

This is how the neurotransmitter that can only affect a receptor molecule sitting on the outside edge of the cell can change the way the cell behaves. Once the receptor activates these other molecules, its mission is complete. The neurotransmitter then is either destroyed or sucked back into the nerve cell that released it. This whole process is called chemical neurotransmission.

Almost all drugs that change the way the brain works do so by tinkering with chemical neurotransmission. Some drugs, like heroin, mimic the effects of a natural neurotransmitter. Others, like LSD, block receptors and thereby prevent neuronal messages from getting through. Still others, like cocaine, interfere with the process by which neurotransmitters are sucked up by the neurons that release them. Others, like caffeine and PCP, exert their effects by interfering with the way messages proceed from the surface receptors into the cell interior.

When drugs interfere with the delicate mechanisms through which nerve cells transmit, receive, and process the information critical for daily living, we lose some of our ability to control our own lives. The continued use of these drugs can actually change the way the brain works. This is the biological basis of addiction.

Observations of people and experiments with animals have taught us that addiction begins when a drug is inappropriately and repeatedly used to stimulate the nerve cells of the pleasure circuit of the brain. Rats hooked up to a drug pump will repeatedly press the lever for doses of illicit drugs that activate dopamine-containing nerve cells in the ventral tegmental area or the neurons that these cells end on in the nucleus accumbens and the frontal cortex. In fact, there is a remarkable similarity between the drugs humans like to abuse and the ones that laboratory monkeys will self administer. Given the opportunity, both monkeys and humans will use cocaine, amphetamines, heroin, alcohol, phenobarbital, nicotine, and virtually every opiate drug. Hallucinogens seem to be the only class of drugs that are preferred only by people.

Animal experiments have taught us that cocaine turns on the pleasure circuit by allowing dopamine to accumulate in the synapses where it is released. Because the amount

| Drug | Human Abuse | Self-Administered By Monkeys |
|---|---|---|
| Cocaine | + | + |
| d-Amphetamine | + | + |
| Fenfluramine | — | — |
| Heroin | + | + |
| Morphine | + | + |
| Fentanyl | + | + |
| Methadone | + | + |
| Buprenorphine | + | + |
| Pentazocine | ? | + |
| Naltrexone | — | — |
| Nicotine | + | + |
| Alcohol | + | + |
| PCP | + | + |
| Diazepam | ± | ± |
| Pentobarbital | + | + |
| Chlorpromazine | — | — |
| Imipramine | — | — |
| LSD | + | — |
| Cannabis | + | — |
| Procaine | — | + |

of dopamine is allowed to build up, strong feelings of pleasure, even euphoria, are elicited. Heroin turns on the pleasure circuit by directly activating opiate receptors on other neurons in this circuit. Even drugs like marijuana, which animals do not like to self administer, can make it easier for other drugs or natural pleasures to turn on the pleasure circuit. This may be why people compulsively use even a relatively weak drug like marijuana.

So, people abuse drugs and animals self administer them because drugs turn on the pleasure center. They do this by altering the normal process of chemical neurotransmission. But, in order to understand why different people use different drugs and how repeated drug use can lead to addiction, it is useful to understand the specific effects of different classes of drugs and the particular brain areas they target.

**Opiates**

This drug class—which includes opium, codeine, morphine, and heroin—comes from the white, milky liquid exuded by the poppy flower. Opium, codeine, and morphine can be extracted directly from the fluid, while heroin is produced by chemically joining two molecules of morphine. Heroin injected into a vein reaches

the brain in a mere 7 or 8 seconds and, because of its chemical structure, penetrates into the brain even faster than morphine, which is probably why most addicts in the United States choose heroin. Once heroin reaches the brain, it quickly binds to the opiate receptors that are found in many brain regions. Activation of the opiate receptors in the pleasure circuit causes intense euphoria, called a rush. This rush lasts only briefly, but is followed by a couple of hours of a relaxed, contented state.

By binding to opiate receptors in other parts of the brain and body, opiates also can stop diarrhea (an important medical use), depress breathing, and cause nausea and vomiting. People who try heroin for the first time often get nauseous or vomit, and some decide they will never use the drug again. But many get past this side effect.

Much more serious is heroin's ability, in large doses, to make breathing shallow or even stop altogether. It does this by binding to opiate receptors that are found on the neurons that control breathing. Activation of these opiate receptors by heroin actually causes the neurons to slow down or stop working altogether. Thousands of people have died because they stopped breathing after a heroin overdose. A number of years ago, however, scientists developed drugs that can block heroin from attaching to opiate receptors. These medications are called opiate antagonists. If someone who has overdosed on heroin is treated with one of these drugs in time, the heroin effects can be completely reversed.

In addition to their many other effects, opiates are the most potent painkillers available. Yet many people who may have had surgery or who are suffering from advanced cancer receive inadequate pain relief because they, their families, or their doctors worry they will become addicted to opiates. But the truth is, this rarely happens. Many studies have shown that pain patients can be treated effectively with strong opiates and either maintained indefinitely or, when their pain is gone, withdrawn from the drug with little problem.

One reason that opiates have so many effects is because opiate receptors are widely distributed throughout the brain and body. The brain also produces its own opiatelike

neurotransmitters, called endorphins, that act just like but more weakly than morphine. Neurons that produce endorphins and neurons that contain opiate receptors are involved in many brain and body functions. The nucleus accumbens contains a large population of opiate receptors, which may be how opiates turn on the pleasure circuit, but regions of the brain involved in emotions and memory—the hippocampus—as well as the cerebral cortex also contain many receptors for opiates.

## Cocaine

Cocaine comes from the leaves of the coca plant, which grows in the mountains of South America. One of the most highly addictive forms of cocaine is crack, a chemically altered form of cocaine that can be smoked. When a person smokes this drug, it enters the brain in seconds and produces a rush of euphoria and feelings of power and self-confidence.

Cocaine, like other stimulants, increases alertness, makes one feel more energetic, and suppresses hunger. In fact, a similar kind of stimulant—the amphetamines—for years were prescribed as appetite suppressants for dieters. One kind of amphetamine, methamphetamine, is now making its way back into illegal use in a smokeable form called ice. This, too, is a highly addictive drug.

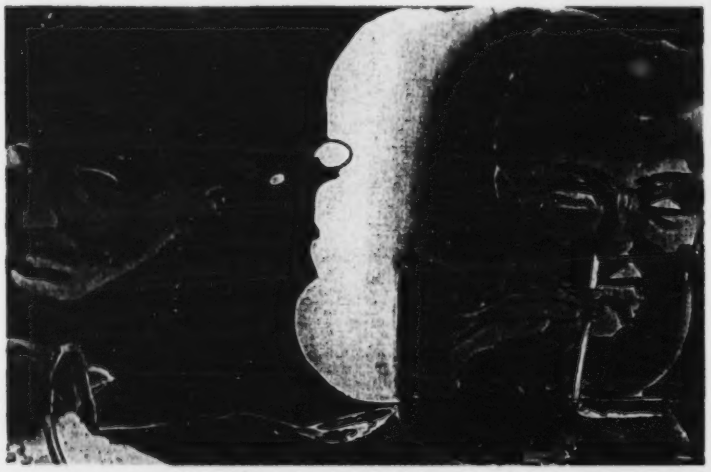
Repeated exposure to stimulants can make a person feel anxious, hyperactive, and irritable. People can become

psychotic, in a way that resembles paranoid schizophrenia, from taking too high a dose of these drugs. For many years, scientists have studied an animal model of psychosis induced by amphetamines to better understand the symptoms of schizophrenia. Finally, a cocaine or amphetamine overdose can cause tremors and lethal brain seizures.

By tracing the path of radioactive cocaine in the brain of human volunteers, researchers have tracked the drug's activity. For a period of up to about 6 minutes, when feelings of euphoria are most intense, cocaine can be found in the frontal cortex regions. After that time, the drug begins to dwindle in that area and is concentrated in another region densely packed with dopamine receptors and axons from dopamine-containing nerve cells.

Because cocaine acts to prevent reabsorption of the neurotransmitter dopamine after its release from nerve cells, cocaine addicts often have higher than normal levels of dopamine in their synapses. This may explain an important finding; the brains of chronic cocaine abusers appear to contain fewer dopamine receptors than normal brains. The excess dopamine causes the neurons that have dopamine receptors to decrease the number of dopamine receptors they make. This phenomenon is called down regulation and may explain the craving for cocaine that occurs during withdrawal from cocaine addiction.

When cocaine is no longer taken and dopamine levels return to their normal, lower concentration, the smaller number of dopamine receptors available for the



neurotransmitter to bind to is insufficient to fully activate nerve cells. Because these nerve cells can no longer do their job, the end result may be such common withdrawal symptoms as depression and a craving for the drug. The depression may reflect the brain's response to the lower level of dopamine action, and the craving is its way of telling the addict to get the dopamine level back up by taking cocaine. This is not unlike the way that hunger motivates us to eat.

**Marijuana and Hallucinogens**

Unlike opiates and stimulants, marijuana and hallucinogens (including LSD and mescaline) alter our perception of reality. These drugs distort the way our senses work and our sense of time, space, and self. In people who are particularly sensitive to them, hallucinogens can produce intense anxiety and even precipitate a psychotic episode.

It is not yet clear exactly how these effects are produced, but radioactive tracing shows that THC, the active ingredient in marijuana, binds to receptors that recognize it. There are many THC receptors in parts of the brain that coordinate movement. This may explain why animals given large doses of marijuana collapse and cannot move.

The hippocampus, a structure involved with the storage of memory, also contains many THC receptors. This may explain why people intoxicated with marijuana have poor short-term memory. Scientists already have shown that chronic administration of THC to rats actually can damage the hippocampus. They are trying to find out if this damage may lead to permanent memory impairment.

**PCP**

This drug has a variety of actions—it is a hallucinogen, a stimulant, and an anesthetic all in one. PCP blocks the way some receptors communicate their message to the inside of the cell and it also blocks certain kinds of receptors. It can produce euphoria, alleviate pain, and lead to disorganized thinking. Depending on the person, PCP can cause drowsiness or aggressiveness and passivity or hostility. A major concern about the drug is the unpredictability of its effects from one time to the next and from one person to the next.

## Depressants

Alcohol may be the most familiar depressant, but this class of drugs also includes tranquilizers like valium and sleeping pills like phenobarbital. A major action of all of these drugs is to reduce anxiety. They may, however, first produce a brief period of excitement or euphoria before they produce calmness, sedation, and sleep.

In higher doses, these compounds can produce anesthesia and relax muscles, and some may serve as anti-seizure medications. In fact, valium and phenobarbital are excellent antiepileptic medicines, but most people find them too sedating for regular use.

People who get drunk may feel alert at first, but then they start to feel depressed and lose their coordination. Most of us have seen the unpleasant and potentially dangerous behavior of drunks. An overdose of alcohol or other depressant can produce stupor and death. Another important effect of these drugs is to impair judgment. People who are drunk often think they are functioning well. This may help to explain why 23,000 people are killed by drunk drivers every year.

## Designer Drugs

So-called "street or basement chemists" have designed a slew of compounds that differ only slightly from the chemical structure of other illegal drugs. Until a few years ago when the laws were changed, these compounds were technically legal, but still had the addictive effects of their chemical cousins. For example, people have modified the stimulant methamphetamine, developing a compound called MDMA, commonly known on the street as ecstacy. It has a combination of stimulant and hallucinogenic properties, but animal studies have shown that it causes a severe, possibly permanent loss of serotonin-containing nerve fibers of the cortex. The Drug Enforcement Administration has declared MDMA illegal.

In general, depending on the origin of the designer drug and how the source drug was modified, the new compound may have widely different properties ranging from stimulant to opiate to hallucinogenic.

Many babies are now being born addicted to cocaine, PCP, or heroin. Normal development of the fetus is a highly complex and intricately timed process that is easily disrupted by drugs. The effects of drugs on the fetus can be absolutely devastating; there is no safe way for a pregnant woman to take drugs.

To understand the effect of drugs on fetal development, consider the opiate receptors in the cortex of the adult and newborn monkey. An adult has three distinct, localized bands of opiate receptors while an infant has only one fairly uniform band.

Newborns actually have many more of these receptors than needed. In the normal course of development in animals, the extra receptors are gradually eliminated because no endorphin-containing nerve fibers contact them. Because they are never activated, they are eliminated. But if a mother is given opiates during her pregnancy, the fetus' opiate receptors all receive constant activation. As a consequence, the receptors do not disappear as they normally would and the normal functioning and continued development of the brain can be disrupted.

Addicted babies are irritable, sensitive, and unusually hard to handle. They appear to have developmental abnormalities as if their brains are trying to get back on track, attempting to develop properly even though they have been thrown off track by drugs. Because normal

development is an exquisitely timed process that builds one event upon another, it is not surprising that drugs can disrupt it so easily.

## The Steps to Addiction

No matter what kind of drug a person is using, nobody begins taking drugs thinking he or she will become addicted. The person says, "I can handle it. I'll just take this a few times and then I'll stop." The fact is, many people can do this. They can experiment with drugs and then stop. But many others cannot. And while we cannot predict who will and who will not get in trouble with drugs, we do know some of the steps along the path to addiction. Knowing the signposts along this route may help people recognize when they have gotten or are about to get into trouble.

Drugs make most people feel good; this is why they want to take drugs more than once or twice. In scientific terms, drug use is a "rewarding behavior" because the high or pleasure it induces tends to reinforce the drug-taking activity. For some people, this reinforcing experience in learning about the pleasures of drug use may lead from experimentation to more regular, social use of a drug. Many people start to use drugs at parties and with friends. Some people stay at this second level of use for many years and never get into trouble. There are, for example, many social drinkers who have never had a problem controlling their level of alcohol consumption.

But for other people, drug use does get out of hand. These people learn to take drugs for emotional support—one person had a tough day, another's boss yelled at her, still another has not done his homework and knows he will be in trouble at school. People get bored, lonely, or just do not like their world very much. Taking drugs to try to solve problems like these helps set the stage for addiction.

At first a person might say; "Well, I didn't do my homework tonight. I feel really guilty, so I'm going to get stoned, forget about it, and go to bed." Then it progresses—snorting cocaine in the stockroom, having a few drinks at lunch, or sneaking a drink or smoking dope in the bathroom to deal with stress. If this continues, physiological changes will begin to take place. Friends may even notice, "You know, he can drink anyone under the table. The guy has a hollow leg." What is happening is that the person has become tolerant to alcohol. If it used to take one or two drinks for that person to get high, after a period of drinking it takes three or four drinks, then five or six. Similarly, the dose needed to get high from marijuana, heroin, or crack also escalates. So the drug user is not only taking drugs more frequently, that person is exposing his or her body to higher doses.

Then, as regular drug use continues, a second related kind of change begins. The body of a habitual drug user begins to need the drug to work normally. The person cannot function without it; when the drug is not available, the person experiences symptoms of withdrawal. Deprived of the drug, the individual may feel anxious, generally lousy, or sick. Using the drug again alleviates these symptoms. Until a person goes into withdrawal, there may be little, if any, evidence that the user is physically dependent on a drug.

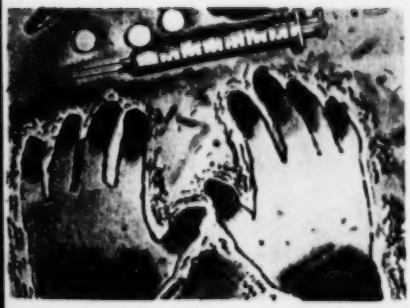
Most importantly, avoiding withdrawal is a powerful force motivating people to keep using drugs. The user now has entered a new stage in his or her relationship with drugs. The user not only needs drugs to produce pleasure, but the person must have them to avoid the pain and discomfort of withdrawal.

But physical dependence is not addiction. For example, people who take opiates to relieve chronic pain can become

physically dependent on their painkilling medication. They would experience withdrawal if they suddenly stopped taking their narcotic. But the drug is not the focus of their existence. Indeed, they use their narcotic medication to live a normal life. Addicts, by contrast, have no life without their drugs. This difference may be why virtually all pain patients have no trouble giving up their opiates if their pain is relieved, while addicts tend to relapse into drug use even after they have been withdrawn and put in treatment for their addiction.

Addiction, then, is more than drug tolerance and physical dependence, though these may be necessary preconditions. Our experience with pain patients has taught us that the defining conditions for addiction also include psychological dependence on the drug. The addicts perceive themselves as chained to the drug and their behavior becomes characterized by compulsive drug-seeking and drug-taking behavior. The focus of life is obtaining drugs, taking drugs, getting high, and then getting more drugs. Everything else—family, friends, job—falls by the wayside. The addict may get fired because he or she cannot function while high; the addict's family may throw the person out because the individual has stolen their money to support a drug habit. At the same time, the addict now needs the drug not only for pleasure, but also to avoid the sick feeling associated with withdrawal. Thus, the addict's ability to choose whether or not to use a drug has been severely compromised because only drugs bring pleasure, the solution to most of life's problems has become drug use, and doing without drugs brings the anxiety and sickness of withdrawal.





Animal studies indicate that the destructive behavior associated with addiction is not unique to humans and thus confirms its biological basis. Rats given free access to cocaine will eventually kill themselves taking it, foregoing even food and drink. They just keep taking cocaine until they die. Some humans stop or seek help before their habit kills them, but others cannot. To make it worse, intravenous drug users run the risk of infecting themselves, their spouses, and their unborn children with AIDS. This fatal disease of the

immune system is increasing most rapidly among intravenous drug users, including prostitutes who shoot up and then spread the disease among their customers.

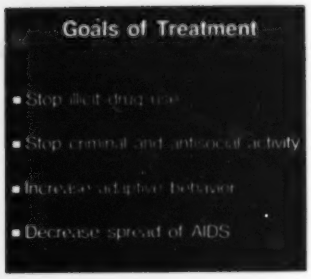
## Treatment

Addicts have a tremendous ability for self-delusion. Some believe and will tell others, "I can stop any time I want. I can handle it." These people are actively denying that their drug problem even exists. But eventually, such people can end up in the emergency room with an overdose, they can get busted selling or buying drugs, or they might even end up on the street rejected by friends and family. Many have to hit some kind of bottom that finally prompts them to seek treatment.

One of the first things to understand about treatment for drug addiction is that it is not a cure. There is no cure for addiction in the way that an ear infection or strep throat can be cured. Drug addiction is a chronic disease that has the potential for relapse. Successful treatment of drug addiction means that the addict significantly reduced use of the drug to which he or she is addicted and that the individual has learned new behaviors that help avoid drug use and other self-destructive activities.

From this perspective, drug addiction can be considered much like hypertension, atherosclerosis, or adult diabetes. These also are chronic diseases that are typically caused by voluntary activities, such as poor diet, poor stress management, and lack of exercise. These diseases cannot really be cured, but they can be controlled through appropriate changes in lifestyle and perhaps with the aid of some medications. Those who treat alcoholics have long recognized the chronic relapsing nature of alcohol addiction; even if an alcoholic has not taken a drink for years, that person is still referred to as "recovering," not "recovered." That is because they know that the potential for relapse always exists and that staying sober requires continuing effort. It is a life-long process. The same is true for any drug addict. The long-term goal in drug addiction treatment is to teach the addict how to live without drugs.

The first goal of any teatment program, however, must be to stop the use of illicit drugs. In order for any treatment


Goals of Treatment
• Stop illicit drug use
• Stop criminal and antisocial activity
• Increase adaptive behavior
• Decrease spread of AIDS

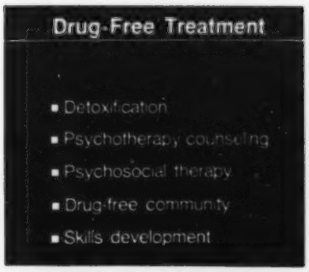
program to work, a person's basic brain biochemistry has to be stabilized and allowed to return to normal so that both the problems that led to drug use in the first place as well as the problems caused by addiction can be addressed. The cessation of drug use often reduces the criminal or antisocial behaviors—including stealing, chronic lying, or the sharing of needles—associated with the drug habit. Often addicts must be taught new skills and habits to replace the destructive behaviors related to addiction.

There are essentially two different approaches that are now used to reach these goals. The first begins with detoxification, the process of removing the addictive substances from the addict's brain and body. This can be done slowly or quickly and often means undergoing withdrawal, though it is possible that the most extreme symptoms can be medically treated. After this process, a drug-free treatment can begin that emphasizes psychotherapy or counseling and group therapy sessions as ways to teach people to solve their problems without resorting to drugs. Many addicts also may have an underlying mental illness that must be treated before effective drug abuse treatment can begin. For otherwise healthy people with a stable family and a job, drug abuse treatments might be successfully undertaken on an outpatient basis.

For people without these social supports, or for those who have been deeply involved in criminal and antisocial activity, residing in a specially designed drug-free community for a year or two may be necessary. These communities typically feature strict control over behavior with rewards for appropriate behavior and punishments for failure to comply with the rules. Such communities not only protect the recovering addict from drugs and the environmental cues that often led to drug use in the past, but they also surround the addict with other people who are undergoing the same recovery process and who can act as role models and lend moral and psychological support.

Skills development, especially for the many adolescent addicts who never learned the social skills necessary to go to school or hold a job, is also critical for continued recovery. Many people have to learn new ways to cope with old problems. They may need remedial education to hold down

a job or attend school; fear or shame about poor reading ability or other inadequate skills may have facilitated the turn to drugs in the first place. Without new skills to deal with the world, relapse into drug use becomes almost inevitable. Drug-free treatments aim to obliterate the old habits associated with drug use and replace those with new coping skills that are essential for a drug-free life.




The alternative to drug-free treatment is medication therapy. Currently, there are only two medications—methadone and naltrexone—that can be used for this type of therapy, and they are both useful only for opiate addicts. It is crucial to note, however, that medications by themselves are not effective treatments for addiction. They must be used as part of a comprehensive treatment program that includes many of the therapeutic activities described above.

Methadone, the best-known maintenance agent, replaces the heroin that addicts are taking. Like heroin, methadone is an opiate agonist, stimulating opiate receptors in the brain. But unlike heroin, which must be injected into a vein four to six times each day to avoid withdrawal, methadone can be taken by mouth and lasts for 24 hours. Instead of repeatedly disrupting brain chemistry, like those repeated shots of heroin do, it stabilizes the brain so an addict can participate in a recovery program. Given in a proper dose, methadone prevents withdrawal and blocks the effects of heroin if the addict should "shoot up" after taking the dose of methadone. It also helps to break the habit of repeatedly injecting drugs and it gets people off needles so their chance of contracting or spreading AIDS goes way down.

Methadone does not produce the intense euphoria associated with heroin and many people have been successfully maintained on methadone for years. These people are able to hold jobs, interact positively with their families, and contribute productively to society. There is little question that when it is properly used, methadone is an effective treatment for some heroin addicts.

Naltrexone is an opiate antagonist; it prevents heroin or other opiates from activating opiate receptors. A person taking naltrexone cannot get high from shooting up heroin. The problem with naltrexone is that most addicts do not

want to take it and now it is used only by highly motivated addicts.

A new addition to some drug treatment programs is deconditioning procedures. Even months after they have stopped using drugs, people with a long history of drug use feel strong urges to use drugs again when they encounter places or situations in which they have used drugs in the past. They have been conditioned to expect to use drugs in those situations just like Pavlov's dogs were conditioned to salivate when they heard a bell that had previously been sounded whenever they received food. Although initially only the food caused salivation, after the food and bell are presented together often enough, the brain learns that the bell means food and the bell itself causes the animal to salivate. This powerful learning mechanism, called Pavlovian conditioning, takes place without us being aware of it and is very difficult to overcome. Deconditioning techniques were developed in animal experiments and are now being applied directly in some treatment programs.

Whether or not a person receives drug-free or maintenance treatment or there is deconditioning, a key component of successful recovery is some form of aftercare that usually includes regular attendance at group meetings with other recovering addicts. These groups, which are largely patterned after Alcoholics Anonymous, supply the support many people need to maintain their drug-free state. One reason they are productive is because addicts can effectively break through the psychological barriers of other addicts. They can best point out the lies that people tell themselves to rationalize their drug behavior, and they can offer poignant support because they are going through the same process of recovery. But whatever form of therapy or aftercare program an addict may use, it is important to understand that treatment can work.



## Drugs, Genetics and Biology

Many people use drugs for years without getting addicted, while others report they felt like an addict the first time they smoked crack. Such observations beg the question: Is there a genetic component to drug addiction? Are some people simply born more vulnerable than others to the effects of drugs? Researchers have found

evidence that at least some alcoholics are genetically predisposed to alcoholism. We do not know if people have a genetic predisposition to become addicted to other drugs, but some addicts report they do not use drugs to get high, but rather to feel normal. It may be they have an inborn chemical imbalance in brain chemistry that is corrected by drugs. Such people might have genetic predispositions to become addicted.

Other suggestive evidence has come from animal studies; rats can be bred either to work for cocaine or to avoid it, or to be dramatically affected by opiates or to have smaller than normal responses to the compounds. These different responses are due to the genetic makeup of the individual strains of animals.

But whether or not some people are genetically vulnerable to drug addiction, it seems clear that biology predisposes us to drug use. Drugs alter the way the brain works by acting directly on our nerve cells. Long-term drug use can lead to long-term changes in brain chemistry. We do not know whether these changes are permanent. Most alcoholics and other recovering addicts know that even one drink or snort of cocaine can lead to an uncontrollable binge of drug use. This suggests that addiction has caused permanent changes in the way the brain responds to drugs.

Because of all we have learned about how drugs affect the brain, scientists now are able to create new medications

that may prevent the drugs from getting a foothold in the brain or that can reverse their effects. Currently, investigators at the National Institute on Drug Abuse and other research institutions are working hard to develop medications that may be used to treat addiction. A drug that can block cocaine's ability to stimulate nerve cells is an important priority. Other drugs that can block the drug hunger or craving, which is a common cause of relapse, also are being sought.

Because of what we have learned from studying both animals and people, it is now clear that addiction is a biologically based disorder of the brain that, like hypertension or diabetes, can be treated with medical and behavioral techniques. As our understanding of the addictive process and its consequences grows, we will continue to create new prevention and treatment techniques to improve our ability to deal with the devastation of addiction.

**Biographical Note**

David Friedman, Ph.D.
Assistant Dean, Basic Sciences Research Development
Associate Professor, Physiology
Bowman Gray School of Medicine
Wake Forest University

David Friedman received his master's degree and doctorate from New York Medical College, where he became an instructor in the department of physiology. He received a National Research Service Award postdoctoral fellowship to work at the Washington University School of Medicine in St. Louis, and joined the National Institute of Mental Health's Laboratory of Neuropsychology in 1980. Dr. Friedman's efforts in neuroscience led him to the field of drug abuse research. In 1983, he joined the Neurosciences Research Branch in the Division of Preclinical Research at the National Institute on Drug Abuse. Four years later he was appointed deputy director of that division. In 1990, he became assistant dean for basic science research development and associate professor of physiology at the Bowman Gray School of Medicine at Wake Forest University.

Dr. Friedman has been a visiting scientist at Johns Hopkins University School of Medicine and guest researcher at the Laboratory of Neuropsychology at the National Institute of Mental Health. He also served on the Public Health Service's Interagency Committee on Pain and Analgesia and as an editorial advisor for *The NIDA Notes* newsletter on drug abuse research.

Clinical Center Communications
National Institutes of Health
NIH Publication No. 91-3172
June 1991



BEST COPY AVAILABLE